

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of DONALD S. ANSON ET AL. Attorney Docket: 604-8
Serial Number: 06/839,215 Group Art Unit: 183
Filed: March 13, 1986 Examiner: J. Kushan
For: FACTOR IX PROTEIN

DECLARATION UNDER RULE 132

DR. JANE GITSCHIER of 44 Vicksbury Street, San Francisco, California, CA 94114 declares as follows:


1. I hold the posts of Assistant Professor Medicine (Genetics) at the University of California, San Francisco and Assistant Investigator at the Howard Hughes Medical Institute, also at the University of California. After obtaining a doctorate in Biology at the Massachusetts Institute of Technology in 1981, I worked as a postdoctoral fellow for Genentech Inc., before joining the University of California in 1985. I am a co-author of the papers "Characterization of the human factor VIII gene" and "Expression of active human factor VIII from recombinant DNA clones", Nature 312, 326-330 and 330-337 (1984) and many other papers relating to the molecular genetics of hemophilia A.
2. I have read the text of the US patent application 06/839,215, the patent examiner's "official action" objecting to the application and his follow-up letter of clarification, and the references mentioned at page 1 lines 20-26 of the patent specification. In the light of these references and any other relevant knowledge which I had at the time of March 15, 1985, I have been asked to answer the following question:

"On the basis of your knowledge and experience in the technical area to which the patent application relates, would you have

- 2 -

expected that a biologically active factor IX protein having a specific activity of at least 90% of that of blood-derived factor IX (and free of contamination by pox virus proteins) could be obtained by recombinant DNA means?"

3. My answer is "no". In my opinion, it was not obvious that the rat hepatoma cell line H4-11-E-C3 (Example 1) would produce a properly processed, fully functional factor IX from a transfected DNA plasmid. Although this cell-line was a good choice for these experiments, as it was known to produce active prothrombin, it was by no means assured that the cell would produce active factor IX from a recombinant plasmid. It was also not assured that it could be produced from a dog kidney cell line (Example 2), as such cells were not known to produce vitamin K or to have any of the other functions necessary to convert the precursor protein into functional factor IX.
4. The undersigned further declares that all statements made herein of her own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.


JANE GITSCHIER

11-17-88

Date